DEPARTMENT OF HEALTH AND HUMAN SERVICES

DMB

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Food and Drug Administration

[Docket No. 01N–0197]

Clinical Development Programs for Drugs, Biological Products, and Devices for the Treatment of Ankylosing Spondylitis (AS) and Related Disorders; Request for Assistance

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is requesting assistance in developing guidance for industry on issues related to drugs, biological products, and devices for the treatment of AS and related disorders. Once finalized, the guidance would aid sponsors and others interested in developing new agents to treat AS and related disorders.

Before the agency can develop such guidance, a critical appraisal of certain fundamentals of the science related to AS is needed. FDA is interested specifically in identifying a party, or parties, willing to take the lead in coordinating this critical appraisal.

DATES: Submit written comments on this notice by [*insert date 60 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Mary Jane Walling, Center for Drug Evaluation and Research (HFD–105), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2268.

SUPPLEMENTARY INFORMATION: Because of the positive response to the agency's guidance on rheumatoid arthritis, the agency has recognized the need for more information on the development

of drugs, biological products, and devices for the treatment of AS and related disorders. FDA intends to put the information received in response to this notice in a public docket so that interested parties can learn of each other and coordinate these activities.

Specifically, the agency is interested in identifying an interested group or consortium of interested groups from academia, industry, practitioners, and patients and their representatives willing to take the lead in a critical appraisal of certain fundamentals of the science related to AS. Initially, the parties may want to organize a public meeting to discuss relevant questions (a number of which are noted below). The agency hopes this meeting will lead to conceptual advances now not present and their expression in a series of concept papers. Subsequent workshops would then be able to fully discuss these concept papers, soliciting feedback from all quarters including regulators from the United States and elsewhere. Emphasis should be on debating the rationale for various approaches to key issues. The agency welcomes other suggestions of activities that could be undertaken as part of this guidance development effort.

To provide a starting point for discussion, the agency has developed a list of some key concepts that the interested parties may want to consider at the meeting:

1. Scope: Should the guidance discuss AS alone, or a broader spondyloarthropathy rubric? What about the clinical subgroups and pediatric expressions of the disorder(s)?

2. Claims: What type of claims structure is optimal to encompass the types of clinical benefit a therapeutic product might have on patients with AS? What type of evidence would be needed to support each proposed claim?

3. Measures of disease activity: Are currently available instruments for measuring disease activity adequate or are new measures required? Which disease activity should be measured in clinical trials in AS, and on what basis: (1) A consensus approach, which aims for agreement (clinicians, patients, and others) based on a blend of an observer-driven approach and performance characteristics; (2) a decision based on the comparative statistical characteristics of each

measurement using concepts such as random measurement error; or (3) a fully data-driven approach where each measurement is tested in a standard venue to assess its predictive capacity.

4. Overall trial design: Are longitudinal comparison of means optimal? Because longer trials inevitably have substantial dropouts, would a survival analysis be more appropriate?

5. Intrinsic trial design: Which measures should be included in the primary analysis of the clinical trial to assess whether the therapeutic product is associated with a clinical benefit? Do all measures need equal-weight in the primary analysis? Can they be unequally weighted? Is the use of composites justified? Are outcomes of secondary endpoints essential for determining the success of the trial?

Interested persons should submit to the Dockets Management Branch (address above) comments and expressions of interest in taking a lead in a critical appraisal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to

be identified with the docket number found in brackets in the heading of this document. Received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: 5/11/01
May 11, 2001.

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Margaret M. Dotzel,
Associate Commissioner for Policy.

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